61. (New) The method of claim 60, wherein said nucleic acid molecule is an RNA molecule.

62. (New) The method of Claim 60, wherein said nucleic acid molecule is a DNA molecule.

REMARKS

Based on the amendments to the claims and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Status of the Claims

Applicants note that the previously pending claims were inadvertently mis-numbered in that number 46 was skipped. Thus, previously pending claims 47-55 should have been numbered 46-54. In the interest of clarity, the previously pending claims have been canceled and new claims numbered 55-62 are presented with claims 55 and 60 being independent claims.

Support for the new claims can be found throughout the specification as filed. No new matter has been introduced.

II. Summary of the Office Action

In the Office Action dated March 26, 2003, the Examiner made 3 rejections of the claims. In addition, the Examiner indicated that previously pending claims 15-17, 39-42, and 44-54 were free of the prior art. Applicants respectfully offer the following remarks to overcome the rejection made in the Office Action.

III. The Rejection of Claims 15-17, 39-42, and 44-54 Under 35 U.S.C. § 112, First Paragraph Must Be Withdrawn

In the Office Action at pages 2 through 11, sections 2 and 3, claims 15-17, 39-42, and 44-54 have been rejected under 35 U.S.C. § 112, first paragraph, as the specification allegedly does not enable one skilled in the art to make and use the

invention commensurate in scope with the claims. The Examiner acknowledges that the specification is enabling "for methods of treatment of human melanoma tumors subcutaneously in humans and mice via administration o[f] the SPARC antisense shown in the specification as filed, and methods [o]f inhibiting SEQ ID NO:1, human SPARC, via administration of said antisense in cells in cell culture (*in vitro*)" but alleges that the specification does not enable the "methods of administration of any SPARC inhibitor for any treatment as broadly claimed." Office Action, page 2. Applicants respectfully request reconsideration and withdrawal of this rejection.

Newly presented claim 55 is drawn to a method of treating a melanoma tumour in a human, comprising administering to cells of said tumour an antisense nucleic acid molecule comprising a sequence that binds to a polynucleotide comprising SEQ ID NO:1 or a corresponding RNA sequence, wherein said nucleic acid molecule has the function of preventing or decreasing expression of human osteonectin. Newly presented claim 60 is drawn to a method of treating a melanoma tumour in a human, comprising administering *in vitro* to tumour cells taken from said human a nucleic acid molecule comprising a sequence selected from the group consisting of nucleotides 15-1698 of SEQ ID NO:1, the reverse complement thereof, an RNA sequence corresponding to nucleotides 15-1698 of SEQ ID NO:1, and an RNA sequence corresponding to the reverse complement thereof, and reintroducing into said human said tumour cells to which said nucleic acid molecule has been administered.

In support of this rejection, the Examiner asserts that "the nearly full-length SPARC antisense taught in the specification as filed is not considered representative of design and use of any other SPARC antisense to SEQ ID NO:1 for the claimed treatment effects since each antisense must be evaluated on an antisense-by-antisense

basis for uses in vivo due to the high level of unpredictability in the art . . .." Office Action, page 5. Applicants respectfully disagree. With regard to claim 55 and claims dependent thereon, the specification provides ample direction as to how to determine whether an antisense nucleic acid molecule decreases or prevents osteonectin expression (*e.g.*, Example 1 and Figure 1) and that this decrease correlates to reduced tumorigenicity (see paragraph bridging pages 18 and 19). Given the teachings of the specification, it would be a matter of routine experimentation to identify antisense oligonucleotides for use in the practice of the claimed invention. With regard to claim 60 and claims dependent thereon, Applicants respectfully submit that this rejection does not apply as the claim recites the full-length antisense referred to by the Examiner.

The Examiner further cites a number of articles detailing the difficulties attendant to the design and use of antisense therapies. Applicants respectfully submit that these difficulties have already been overcome by the present invention in the treatment of melanomas as presently claimed. The specification provides a working *in vivo* model system that demonstrates the efficacy of the presently claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection as it may be applied to the present claims.

IV. The Rejection of Claims 15-17, 39-42, and 44-54 Under 35 U.S.C. § 112, First Paragraph Must Be Withdrawn

In the Office Action at pages 11 to 13, section 4, claims 15-17, 39-42, and 44-54 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to convey to one skilled in the art that the applicants were in possession of the claimed invention at the

time the application was filed. Applicants respectfully request reconsideration and withdrawal of this rejection.

In support of this rejection, the Examiner asserts:

> [t]he description of one antisense having a correlated treatment function to decrease melanoma cancer subcutaneously is not considered representative of a representative number of species of any SPARC inhibitor (antisense, ribozyme, or other type) as broadly claimed having the breath [sic] of treatment effects in a whole organism upon administration. As reiterated above, "[a] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence . . ." Absent further specific nucleic acid sequence description that directly correlates to the claimed treatment effects, one of skill in the art would not readily envisage the nucleic acid sequence structure of any other SPARC nucleic acid inhibitor having the claimed treatment functions upon administration to a whole organism.

Office Action, page 12.

Applicants do not agree with the Examiner's characterization of the teachings of the specification and believe that the specification as filed conveys to those skilled in the art that Applicants were in possession of the claimed invention at the time of filing. For example, the specification provides a discussion of ribozyme techniques and directs the skilled artisan to numerous publications that discuss the techniques in greater detail (see pages 15 and 16). Nonetheless, in the interests of advancing the prosecution of the present application, the newly presented claims are directed to antisense nucleic acid molecules that bind to SEQ ID NO:1. Thus, the portion of this rejection directed to other treatment modalities (*e.g.*, ribozymes, etc) is not germane. Applicants specifically reserve the right to prosecute claims to these other treatment modalities in continuing applications.

With regard to the portion of this rejection in which the Examiner asserts that the biomolecule sequence is characterized solely by function without disclosed correlation between that function and the structure of the sequence as it may be applied to claim 55 and claims dependent thereon, Applicants respectfully submit that the specification does provide the correlation between the function and the structure. The entire sequence of the osteonectin cDNA is provided. This provides one skilled in the art with the necessary structure in order to design antisense molecules that have the desired function of preventing or decreasing expression of human osteonectin. With regard to newly presented claim 60 and claims dependent thereon, Applicants submit that this rejection does not apply as the claim specifically recites the structure of the claimed nucleic acid molecules. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection as it may be applied to the newly presented claims.

V. The Rejection of Claims 6-8, 37, 43, and 55 Under 35 U.S.C. § 103(a) as Being Unpatentable Over Ledda, in view of GenEmbl Accession No. J03040, Baracchini, and Ostrand-Rosenberg Must Be Withdrawn

In the Office Action at pages 13-16, sections 5 and 6, claims 6-8, 37, 43, and 55 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ledda, *et al.*, (*Medicina* Vol. 55:565-566, Abstract No. 267, Sociedad Argentina De Investigacion clinica, December 1995), in view of GenEmbl database Accession No. J03040 (human SPARC/osteonection mRNA, complete CDS., January 1995), Baracchini *et al.* (US patent no. 5,801,154), and Ostrand-Rosenberg *et al.* (US patent no. 5,858, 776). As these claims have been canceled, Applicants respectfully request reconsideration and withdrawal of this rejection.